Andt Chins 11/20/03

11-20-03 03:17pm From-PILLSBURY WINTHROP CARMEL VLY.

858 509 4010

T-361 P.010/028 F-410

018813-0272487

Amendments to the Claims

This listing of claims will replace all prior versions and listing of claims in the application.

Claims 1 to 269 (cancelled).

270. (Currently amended) An isolated protein having anticoagulant activity and having one or more <u>Nematode-extracted</u>

<u>Anticoagulant Protein domains ("NAP domains")</u>, wherein each NAP domain includes the sequence:

Cys-Al-Cys-A2-Cys-A3-Cys-A4-Cys-A5-Cys-A6-Cys-A7-Cys-A8-Cys-A9-Cys-A10 (FORMULA III), wherein

- (a) Al is an amino acid sequence of 7 to 8 amino acid residues;
 - (b) A2 is an amino acid sequence;
- (c) A3 is an amino acid sequence of 3 amino acid residues and has the sequence Asp-A3_a-A3_b wherein A3_a and A3_b are independently selected;
- (d) A4 is an amino acid sequence having a net anionic charge;
- (e) A5 is an amino acid sequence of 4 amino acid residues and has the sequence A5_a-A5_b-A5_c-A5_d (SEQ. ID. NO: 85), wherein A5_a through A5_d are independently selected amino acid residues;
 - (f) A6 is an amino acid sequence;
- (g) A7 is an amino acid residue selected from the group consisting of Val and Ile;
- (h) A8 is an amino acid sequence of 11 to 12 amino
- (i) A9 is an amino acid sequence of 5 to 7 amino acid residues; and

- (j) Al0 is an amino acid sequence; wherein each of A2, A4, A6 and Al0 has an independently selected number of independently selected amino acid residues and each sequence is selected such that each NAP domain has in total less than about 120 amino acid residues, and wherein the protein has a NAP domain with an amino acid sequence substantially the same as having at least 90% homology with the NAP domain of AcaNAPc2 (SEQ. ID. NO: NO: 59).
- 271. (Currently amended) An isolated protein having anticoagulant activity and having one or more NAP domains, wher each NAP domain includes the sequence:

Cys-A1-Cys-A2-Cys-A3-Cys-A4-Cys-A5-Cys-A6-Cys-A7-Cys-A8-Cys-A9-Cys-A10 (FORMULA III), wherein

- (a) Al is an amino acid sequence of 7 to 8 amino acid residues;
 - (b) A2 is an amino acid sequence;
- (c) A3 is an amino acid sequence of 3 amino acid residues and has the sequence Asp-Lys-Lys;
- (d) A4 is an amino acid sequence having a net anionic charge;
- (e) A5 is an amino acid sequence of 4 amino acid residues and has the sequence $A5_a-A5_b-A5_c-A5_d$ wherein $A5_a$ is Leu, $A5_c$ is Arg and $A5_b$ and $A5_d$ are independently selected amino acid residues (SEQ. ID. NO: 357);
 - (f) A6 is an amino acid sequence;
 - (g) A7 is Val;
- (h) A8 is an amino acid sequence of 11 to 12 amino acid residues and includes the amino acid sequence A8_a-A8_b-Gly-Phe-Tyr-Arg-Asn (SEQ. ID. NO: 79), wherein at least one of A8_a and A6_b is Glu or Asp;

- (i) A9 is an amino acid sequence of 5 to 7 amino acid residues; and
- (j) Al0 is an amino acid sequence; wherein each of A2, A4, A6 and A10 has an independently selected number of independently selected amino acid residues and each sequence is selected such that each NAP domain has in total less than about 120 amino acid residues, and wherein the protein has a NAP domain with an amino acid sequence substantially the same as having at least 90% homology with the NAP domain of AcaNAPc2 (SEQ. ID. NO: NO: 59).
- 272. (Currently amended) An isolated protein having Factor VIIa/TF inhibitory activity having a NAP domain with an amino acid sequence substantially the same as having at least 90% homology with the NAP domain of AcaNAPc2 (SEQ. ID. NO: 59).
- 273. (Currently amended) An isolated protein having an amino acid sequence substantially the same as having at least 90% homology with AcaNAPC2 (SEQ. ID. NO. 59).
- 274. (Currently amended) An isolated protein having an amino acid sequence substantially the same as having at least 90% homology with AcaNAPc2/proline.
- 275. (Previously presented) A method of treating a pathologic condition characterized by abnormal thrombosis by preventing or decreasing the abnormal thrombosis which comprises administering a protein of claim 270.
- 276. (Previously presented) A method of treating a pathologic condition characterized by abnormal thrombosis by preventing or decreasing the abnormal thrombosis which comprises administering a protein of claim 271.

018813-0272487

- 277. (Previously presented) A method of treating a pathologic condition characterized by abnormal thrombosis by preventing or decreasing the abnormal thrombosis which comprises administering a protein of claim 272.
- 278. (Previously presented) A method of treating a pathologic condition characterized by abnormal thrombosis by preventing or decreasing the abnormal thrombosis which comprises administering a protein of claim 273.
- 279. (Previously presented) A method of treating a pathologic condition characterized by abnormal thrombosis by preventing or decreasing the abnormal thrombosis which comprises administering a protein of claim 274.
- 280. (Previously presented) A method according to any one of claims 275 to 279 wherein said pathologic condition is disseminated intravascular coagulopathy.
- 281. (Previously presented) A method according to any one of claims 275 to 279 wherein said abnormal thrombosis occurs in the venous vasculature of patients undergoing major surgery in the lower extremetics extremities or abdominal area.
- (282. (Previously presented) A pharmaceutical composition comprising a protein of any one of claims 270 to 274 and a pharmaceutically acceptable carrier.